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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,621	09/10/2003	Michael Ian Phillips	5853-257	5561

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EXAMINER
GUZO, DAVID

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,621	PHILLIPS ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/3/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 18-22* is/are rejected.

7)☒ Claim(s) *16 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The filing date of the 60/409,688 application is incorrectly listed, in the Declaration, as September 10, 2002 rather than the actual date of September 11, 2002.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 9, 18-20 and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Phillips et al.

Applicants claim a system (which can be at least one cell *in vitro* or *in vivo*) for expressing a heterologous gene in a cell type-specific and inducible manner, the system comprising at least one vector (which can be an AAV vector) comprising a nucleic acid encoding a switch/biosensor, a nucleic acid encoding a tissue-specific promoter, a nucleic acid encoding the heterologous gene, and a nucleic acid encoding a gene amplification component (comprising a transactivator and regulatory element), wherein

the switch/biosensor allows the system to regulate expression of the heterologous gene in response to a stimulus, the tissue-specific promoter allows the system to selectively express the heterologous gene in a particular cell type, and the gene amplification component induces expression of the heterologous gene at a level sufficient to exert a detectable physiological effect on a cell administered the system. Applicants also claim a method for expressing a heterologous gene in a cell (which can be in an animal) in a cell type-specific and inducible manner, the method comprising administering to the cell at least one vector comprising a nucleic acid encoding a switch/biosensor, a nucleic acid encoding a tissue- specific promoter, a nucleic acid encoding the heterologous gene, and a nucleic acid encoding a gene amplification component, wherein the switch/biosensor allows the system to regulate expression of the heterologous gene in response to a stimulus, the tissue-specific promoter allows the system to selectively express the heterologous gene in a particular cell or tissue type, and the gene amplification component induces expression of the heterologous gene at a level sufficient to exert a physiological effect on a cell administered the system.

Phillips et al. (Hypertension, Feb 2002, Vol. 39(Part 2), pp. 651-655, see whole article, particularly the Abstract, Fig. 1, p. 652 and Discussion section) teaches the same "vigilant vector" system as claimed by applicants in the instant application. As shown in Fig. 1 (p. 652) the "vigilant vector" system disclosed by Phillips et al. includes a switch/biosensor (i.e. HRE) operably linked to a tissue specific promoter (which can be MLC-2v) operably linked to a therapeutic gene of interest. The system also comprises a gene amplification component (sequence encoding HIF-1α) which induces

expression of the heterologous gene of interest at a level sufficient to exert a detectable physiological effect on the cell. The vectors disclosed by Phillips et al. are designed to be used to infect cells *in vivo* to express therapeutic genes (i.e. genes for cardioprotection against ischemia). Phillips et al. therefore teaches the claimed invention.

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-8, 10-15 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips et al. in view of Tang et al.

Applicants' invention is as recited in the above 35 USC 102(a) rejection. Additionally, applicants recite that the transactivator comprise a GAL4 DNA binding domain and a p65 activation domain and wherein the regulatory element comprises a GAL4 UAS and an Ad E1b TATA element. Also, applicants recite that the "vigilant vector" system is on two rAAV vectors and a method for expressing a heterologous in a cardiac myocyte comprising use of the claimed "vigilant vector" system.

Phillips et al. is applied as above. Phillips et al. does not teach that the transactivator comprise a GAL4 DNA binding domain and a p65 activation domain, the regulatory element comprises a GAL4 UAS and an Ad E1b TATA element, the "vigilant vector" system being on two rAAV vectors and a method for expressing a heterologous in a myocyte comprising use of the claimed "vigilant vector" system. Phillips et al. appears to specifically refer to the Tang et al. paper (applied below) in the paragraph bridging pp. 653-654 and indicates that incorporation of a chimeric transcription factor consisting of GAL4 DNA binding domain and the p65 transactivation domain increased reporter gene by 400-fold when activated by hypoxia.

Tang et al. (Hypertension, Feb. 2002, Vol. 39 (Part 2), pp. 695-698, see whole article, particularly the Abstract, Fig. 1, "Methods" section pp. 695-696 and "Discussion" section) recites a "vigilant vector" system comprising a transactivator comprising a GAL4 DNA binding domain and a p65 activation domain and wherein the regulatory element comprises a GAL4 UAS and an Ad E1b TATA element.

The ordinary skilled artisan, seeking to improve the "vigilant vector" system recited by Phillips et al., would have been motivated to modify the "vigilant vector"

system disclosed by Phillips et al. by incorporating a transactivator comprising a GAL4 DNA binding domain and a p65 activation domain and wherein the regulatory element comprises a GAL4 UAS and an Ad E1b TATA element, as disclosed by Tang et al., because Phillips et al. specifically refers to the teachings of Tang et al. and indicates the desirability of using the transactivator system disclosed by Tang et al. in order to increase expression of the gene of interest. It would have been obvious for the skilled artisan to combine the teachings of Phillips et al. with the teachings of Tang et al. because Phillips et al. specifically recites the teachings of Tang et al. and the desirability of using said teachings to improve the "vigilant vector" system disclosed by Phillips et al.

With regard to the "vigilant vector" system being divided onto two rAAV vectors, Phillips et al. teaches a single rAAV vector but also teaches that a two vector system (as disclosed by Tang et al.) can be used to construct a "vigilant vector" system. The ordinary skilled artisan would have been motivated to modify the "vigilant vector" system disclosed by Phillips et al. and Tang et al. by using two rAAV vectors because Phillips et al. teaches that AAV vectors have desirable characteristics of being safe *in vivo* and being stable for long periods of time. It would have been obvious for the ordinary skilled artisan to use rAAV vectors for all parts of the "vigilant vector" system because Phillips et al. teaches that AAV vectors are desirable for use *in vivo* and because the ultimate use of the "vigilant vector" system is *in vivo* for cardioprotection against ischemia. The ordinary skilled artisan would therefore be motivated to choose a vector system, for the 'vigilant vector" constructs that was demonstrated safe *in vivo*.

With regard to use of the instant "vigilant vector" system to express genes in cardiac myocytes, it is noted that the heart contains primarily myocyte cells and any cardiac treatment protocol (i.e. for cardioprotection against ischemia) using the instant vector system would require the vectors to transfect cardiac myocytes in the heart.

Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 16-17 are free of the art because the art does not teach the specific first and second rAAV constructs comprising the switch/biosensor, the tissue-specific promoter, and transactivator encoded by nucleic acids comprised on a first rAAV vector, and the regulatory element and the heterologous gene encoded by nucleic acids comprised on a second rAAV vector and optionally a third rAAV vector comprising a regulatory element operably linked to a transgene differing from the heterologous gene.

No Claims are allowed.

Claims 16-17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571)

272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
August 1, 2006

DAVID GUZO
PRIMARY EXAMINER